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Case Report

Use of Intravitreal Dexamethasone in a Case of Anterior Ischemic Optic Neuropathy

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Keywords
Nonarteritic anterior ischemic optic neuropathy · Intravitreal injection · Dexamethasone

Abstract
Nowadays there is no unique and well-established treatment for nonarteritic anterior ischemic optic neuropathy, despite being the main acute pathology that affects the optic nerve in the elderly population and often resulting in a significant loss of visual acuity. The effectiveness of oral steroids is still under debate in the international literature, although many studies show that patients treated with high doses of systemic corticosteroids have a significantly higher chance of improved visual acuity and visual fields. The authors propose an intravitreal dexamethasone injection/implant as initial and acute therapy. Compared to systemic corticosteroids, intravitreal dexamethasone has the advantage of avoiding any systemic side effects of steroids. On the other hand, a rise in intraocular pressure might occur, manageable with local antiglaucoma drugs, especially in patients at risk, and there is a risk of induced cataract. The pharmacodynamics of the intravitreal dexamethasone slow-release implant is characterized by a first step with high release concentrations and a second following phase with decreasing concentrations. Therefore, the use of emergency dexamethasone (high concentration) intravitreal injection is justified as a treatment after the first detection of an ischemic optic anterior neuropathy.

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Case Report

The purpose of our study is to evaluate indications and prospects of the use of intravitreal dexamethasone slow-release implantations – containing 0.7 mg (700 μg) – in the case of nonarteritic anterior ischemic optic neuropathy, especially in the acute phase and in the possible prevention of the same disease in the fellow eye. For arteritic anterior ischemic optic neuropathy, the doses of systemic corticosteroid could be reduced.

An 83-year-old woman with arterial hypertension, in therapy with Cardioaspirin, came to our attention. She reported a previous anterior ischemic optic neuropathy in her right eye with low vision (3/50) in 2005. She was pseudophakic in both eyes. She went to the emergency room due to a decrease of visual acuity in her left eye. Her right eye visual acuity was 4/50 with refractive correction, and her left eye visual acuity was 3/50 with refractive correction. Moreover, she reported a hospitalization on April 4–8, 2014, 1 week before presenting to the emergency room, due to papilledema in her left eye, which was treated with intramuscular betamethasone 4 mg q.d. for 5 days, then with oral prednisone 5 mg b.i.d. for 5 days (left eye visual acuity was 4/50 with correction on the last day of hospitalization). We obtained a magnetic resonance image, fluoroangiography (Fig. 1), doppler ultrasonography, the visual evoked potentials (Fig. 2), and optical coherence tomography. Automated perimetry could not be performed due to low vision. We decided to treat her with an intravitreal dexamethasone injection/implant.

Follow-up visits on days 1, 7, and 30 from the intravitreal injection consisted of measuring visual acuity, performing tonometry and fundus examination with slit lamp, and, on day 30, performing automated perimetry (30/2; Fig. 3), optical coherence tomography, measuring visual evoked potentials, and performing fluoroangiography. Thirty days after the intravitreal dexamethasone injection (in the left eye), the left eye visual acuity was 2/10 with refractive correction. Visual field improvements are also provided (Fig. 3).

Discussion

Nowadays there is no unique and well-established treatment for nonarteritic anterior ischemic optic neuropathy, despite being the main acute pathology that affects the optic nerve in the elderly population and often resulting in significant loss of visual acuity [1].

The initial visual acuity is less than 20/400 in 19% of patients, between 20/40 and 20/400 in 43%, and more than 20/40 in 38% [2]. In a recent cohort study, Hayreh and Zimmerman [3] showed that of 386 eyes studied, at the initial visit, in eyes seen ≤2 weeks from the onset of symptoms, 49% had a visual acuity of ≥20/30 and 23% had ≤20/200; in these eyes, 38% had minimal to mild visual field defect and 43% marked to severe defect. Furthermore, visual acuity and visual fields showed improvement or further deterioration mainly up to 6 months, with no significant change after that [3]. A subsequent attack in the fellow eye is estimated to occur in 15–25% of patients with nonarteritic ischemic optic neuropathy [4].

The effectiveness of oral steroids is still under debate in the international literature, although many studies show that patients treated with high doses of systemic corticosteroids have a significantly higher chance of improved visual acuity and visual fields [5]. The surgical decompression of the optic nerve seems to have no benefit and may even be harmful [6, 7], and surgical risks are involved.

The main purpose of the initial treatment is to exclude temporal arteritis, because it is treatable with corticosteroids, and to control systemic factors, such as hypertension and diabetes mellitus. In the future, arteritic ischemic optic neuropathy will also be treatable with intravitreal injections of dexamethasone to avoid systemic side effects and to better control corticosteroid-dependent systemic pathologies, such as hypertension and/or diabetes mellitus.

Some authors proposed the use of intravitreal injections of triamcinolone and of anti-VEGF off-label [8–10] obtaining conflicting results, with a resolution of the disc edema and an improvement of visual acuity, but not of visual fields, or with improvement of visual acuity but not a long-term one.

Alten et al. [1] proposed the use of intravitreal dexamethasone injections because the injection of intravitreal steroids can reduce the vascular loss in the optical disc, facilitate the resolution of the edema of the disc, reduce capillary compression, and eventually improve the hypoxia survival rate of the retinal nerve fiber layer. The anterior ischemic neuropathy develops a cycle consisting of ischemia, edema, and development of a compartment syndrome that leads to increased tissue loss. The reduction of disk edema can increase the reversible component of ischemic damage and axoplasmatic flow. Histopathological studies have shown that the number of macrophages in the areas affected by hypoxic injury increase over time [11].

In a rodent model of nonarteritic anterior ischemic optic neuropathy treated with an intravitreal injection of triamcinolone acetonide, Huang et al. [12] showed a decrease in microglial infiltration in the optic nerve and a decrease of the number of apoptotic cells in the retinal ganglion cell layer.

Many authors proposed the use of intravitreal dexamethasone in patients with macular edema due to branch or central retinal venous occlusion, obtaining effective and safe results, with the exception of a progression of cataracts [13].

Compared to systemic corticosteroids, intravitreal dexamethasone has the advantage of avoiding any systemic side effects of the steroids. On the other hand, a rise in intraocular pressure might occur, manageable with local antiglaucoma drugs, especially in patients at risk, and there is a risk of induced cataract, but a cataract can also develop after systemic corticosteroid therapies and in both eyes.

The pharmacodynamics of intravitreal dexamethasone slow-release implantation is characterized by a first step with high-release concentrations and a second following phase with decreasing concentrations [14]. Therefore, the use of emergency dexamethasone – 0.7 mg (700 μg) – intravitreal injection/implant is justified as an immediate treatment after the first detection of ischemic optic anterior neuropathy.

The second kinetic phase of the drug may also be useful in preventing an attack of the same disease in the fellow eye. It was established that the risk of recurrence in the fellow eye is 12–15% at 5 years and seems to be greater in case of diabetes, while it is not related to gender, age, smoking status, or use of aspirin [15].

The use of intravitreal dexamethasone slow-release implantations (0.7 mg; 700 μg) opens interesting prospects for the treatment of anterior ischemic optic neuropathy, in the acute phase or not.

There are 5 aspects to emphasize and highlight in the development of a protocol with clinical significant evidence and adequate therapeutic results: the first is related to the timely start of treatment – no more than 2–4 h after onset and early diagnosis; the second is directly proportional to the repetition of the treatment of intravitreal dexamethasone, 1 or 3 months after the first injection – to be evaluated on a case by case basis; the third is in rela-

tion to the combination of retrobulbar injection of triamcinolone; the fourth to the treatment of the contralateral eye – because of the high risk of involvement – with both intravitreal dexamethasone implantation or retrobulbar triamcinolone – to be evaluated on a case by case basis, and the fifth to correlate intravitreal autologous stem cells graft – consequently to intravitreal dexamethasone implantation – with a neuroprotective and neuroregenerative effect.

This surgical ocular technique can be used/standardized in emergencies, not only for acute optic nerve pathologies, but also for acute corioretinal vascular pathologies or in association.

In the future, assessment and improvement of different types of dexamethasone on the market that improve the minimum effective concentration and the kinetic drug are needed.

Statement of Ethics

This study followed the tenets of the Declaration of Helsinki. Personal identifiers were removed because consent to publishing such information was not obtained.

Disclosure Statement

The authors have no conflicts of interest to disclose. This is an unfunded study.

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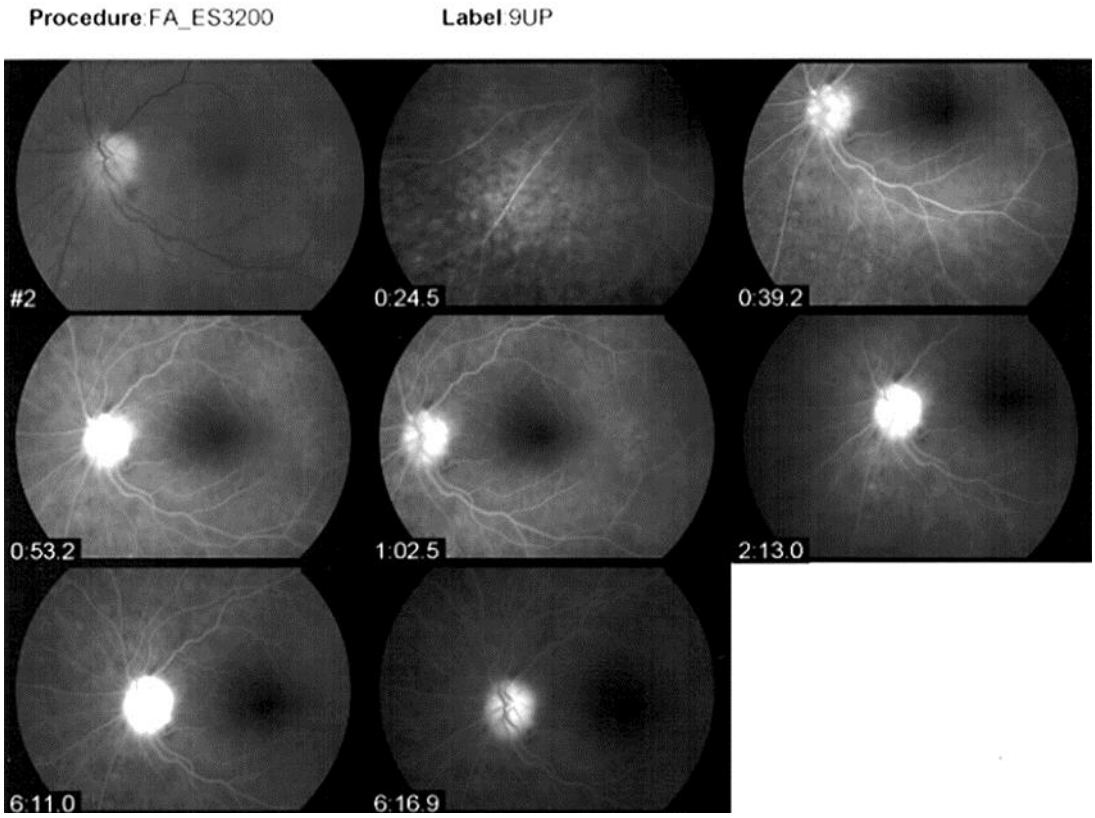

Fig. 1. Fluoroangiography: left-eye papillary hyperfluorescence in early phases.

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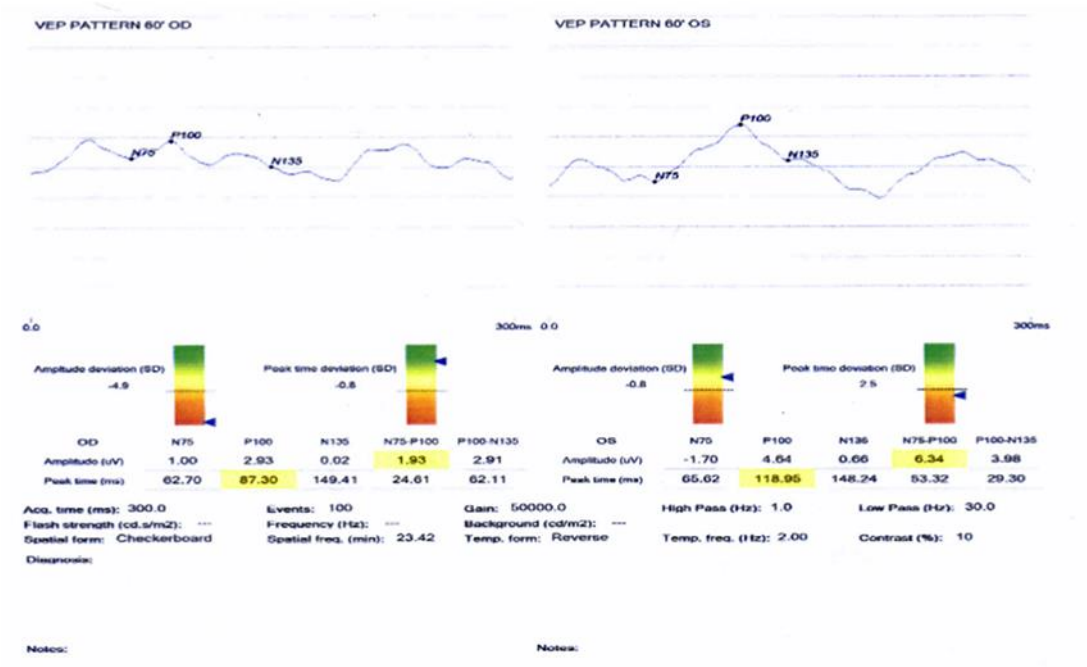

Fig. 2. Visual evoked potentials.

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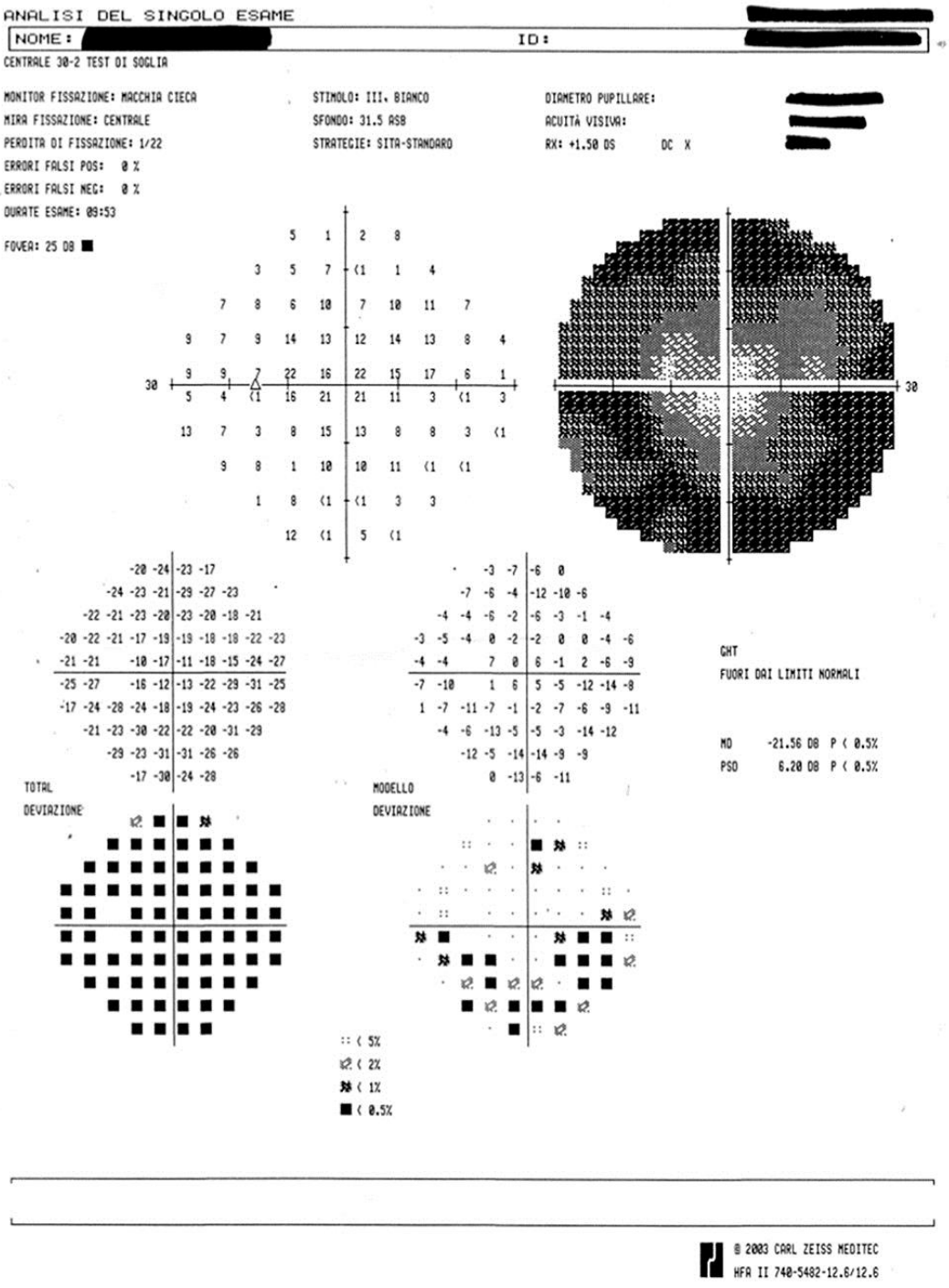

Fig. 3. Automated perimetry 30/2, 30 days after intravitreal dexamethasone implant.